Nigella Sativa
A Panacea for Human Disease  By Philip Rouchotas MSc, ND, and Heidi Fritz MA, ND

Abstract
Nigella sativa, also known as black cumin, is a highly-regarded and prominent herb that has been used in traditional Middle Eastern and Indian systems of medicine. The Prophet Muhammad was recorded as stating that the herb can cure any disease, other than death. Many therapeutic activities have been ascribed to Nigella, including astringent, bitter, stimulant, anthelmintic, carminative, anodyne, expectorant and other effects. In modern research, Nigella has been shown to possess potent anti-inflammatory activity, lipid, glucose, and blood pressure lowering effects, anti-allergic effects, as well as neuroprotective, antimicrobial, and smooth muscle relaxing effects. Preclinical research has indicated potentially important anticancer effects, though this has yet to be investigated in human studies. These effects have been attributed in large part to the constituent thymoquinone. This long list of therapeutic effects demonstrated by scientific research reinforces the traditional view of this impressive herb.

Introduction
Nigella sativa, also known as black cumin, is part of the Ranunculaceae family and an herb with a long history of traditional use in southeast Asia, Egypt, Greece, and the Middle East (Khan 2011). Nigella was regarded as a panacea by the ancients, and played a central role in the medical practice of Middle Eastern and South Asian societies for over 2000 years, where it was used for the treatment of a range of conditions including asthma, headache, dysentery, infection, back pain, dermatological and gastrointestinal conditions (Isik 2010). In traditional Indian medicine, Nigella seeds are astringent, bitter, stimulant, diuretic, emmenagogue, anthelmintic, galactogogue, carminative, anodyne, sudorific, febrifuge, expectorant, purgative, and abortifacient (Parrakh 2010). The medieval Islamic philosopher Avicenna wrote of Nigella in his Canon of Medicine, that it stimulates the body’s energy and helps recovery from fatigue and dispiritedness (Parrakh 2010). Mohammed is reported to have said that the seed has the power to cure every disease except death (Parrakh 2010).

Medically, Nigella has been used in the form of crushed seed, oil, and water extract. The activity of Nigella has been attributed to its thymoquinone content, which is present in both the fixed and essential oils of Nigella; thymoquinone has been extracted and used therapeutically in isolation (Akhondian 2011, Paarakh 2010).
Nigella oil also contains plant sterols, as well as 25% oleic acid, 55% linoleic acid, nigellone, and volatile oils including thymol, limonene, and carvacrol (Işık 2010, Paarakh 2010). It is also possible that fibre content may mediate part of the metabolic effects of Nigella.

Mechanism of Action: Preclinical Evidence

There is a wealth of information on Nigella and thymoquinone derived from preclinical research. Thymoquinone appears to be capable of protecting tissues and organs from various types of damage due to anti-inflammatory and antioxidant activity, and has also been investigated for its anticancer effects (Woo 2012). In animal models of diabetes, thymoquinone was shown to inhibit cellular expression of the COX-2 enzyme and increased levels of the antioxidant enzyme superoxide dismutase (Al Wafai 2013). In models of hyperlipidemia, Nigella sativa volatile oil and methanol extract have both been shown to reduce triglyceride and increase HDL, as well as decrease hepatic HMG-CoA reductase activity (Ahmad 2013). In smooth muscle tissue, including intestinal and bronchial tissue, thymoquinone has been shown to inhibit spontaneous contraction via inhibition of voltage-gated calcium channels (Ghayur 2012). Thymoquinone has also been shown to inhibit liver fibrosis (Bai 2013); attenuate lung injury and fibrosis (El-Khouly 2012); attenuate diabetic nephropathy (Sayed 2012); prevent E. coli induced tissue damage in bacterial prostatitis (Inci 2013); and prevent dextran sulfate sodium-induced colitis (Lei 2012).

In an animal model of epilepsy, thymoquinone was shown to have antioxidant effects in attenuating malondialdehyde (a marker of lipid peroxidation), reduced neurodegenerative changes and neuron loss, and decreased the number of reactive astrocytes (astrogliosis) (Dariani 2013). Thymoquinone has also been shown to have protective effects against amyloid β-induced neurotoxicity, leading to the suggestion that Nigella may have therapeutic potential in Alzheimer’s disease (Alhebshi 2013).

Nigella and its constituent thymoquinone have also been extensively studied in lab models for its anticancer effects. Thymoquinone has been shown to have pro-apoptotic effects in breast cancer, including synergistically with tamoxifen (Rajput 2013); and has been shown to inhibit cancer cell growth and invasiveness in lung, liver, colon, melanoma, and breast cancer cells (Attoub 2012). This is an area where further research is needed to investigate these promising activities.

Clinical Trials

There is a well-developed body of evidence investigating Nigella in humans. Nigella has been shown to have anti-diabetic, blood pressure and cholesterol lowering effects. It also has activity against specific types of infection, possesses anti-allergic effects, and improves rheumatoid arthritis as well as pediatric seizures. Table 1 summarizes all available evidence from human intervention trials concerning the herb as identified through Pubmed and Google Scholar.

In metabolic syndrome, Nigella seed has been shown to significantly decrease total cholesterol, LDL, and triglyceride (Dehkordi 2008, Sabzghabaei 2012), improve fasting and post-prandial glucose and HbA1C (Bamosa 2010), decrease systolic blood pressure (Datau 2010, Dehkordi 2008) by almost 10 points in one study (Datau 2010), as well as promote reduction of body weight and waist circumference (Datau 2010). In the area of allergy and asthma, Nigella oil or extract has been shown to significantly reduce symptoms of allergic rhinitis (Kalas 2003, Nikakhlagh 2011), as well as reduce the severity and frequency of asthma symptoms, improve lung function tests, and reduce the need for asthma medications (Boskabady 2007). Also related to respiratory function are two studies showing that Nigella can act as an antimicrobial agent in acute pharyngitis (Dirjomuljono 2008), and improve lung function, respiratory symptoms, as well as medication requirements in patients who were victims of chemical warfare (Boskabady 2008). One study found that Nigella seed in combination with omeprazole was equal to triple therapy in the eradication of H. pylori (Salem 2010). Finally, one study each showed that Nigella was effective in reducing disease activity of rheumatoid arthritis (Gheita 2012), and reduce the frequency of seizures in patients with refractory epilepsy (Akhondian 2011).

Dosage

The effective dosage forms and quantities of Nigella used include 2g of ground seeds in metabolic syndrome or syndrome components (Sabzghabaei 2012); 1-4g seed oil for inflammatory conditions such as...
### Table 1. Human clinical trials of Nigella sativa

<table>
<thead>
<tr>
<th>Indication</th>
<th>Design</th>
<th>Dose</th>
<th>Outcome</th>
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<td><strong>Metabolic syndrome</strong></td>
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<td>Hyperlipidemia</td>
<td>RCT; N=88 subjects with TC&gt;200 mg/dL</td>
<td>2g crushed Nigella seeds or placebo (in 500mg caps) x4wk</td>
<td>Significant decreases in: TC by 4.78%; LDL by 7.6%; TG by 16.65%. No change in fasting glucose or HDL.</td>
<td>Sabzghabaee 2012 [Abstr]</td>
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<td>Metabolic syndrome</td>
<td>RDBPCT; N=40 obese men with no more than stage I hypertension and normal or impaired glucose</td>
<td>1.5g Nigella seed or placebo twice daily x 3mo</td>
<td>Body weight, waist circumference, and systolic blood pressure decreased in the Nigella group only (p&lt;0.05 for all compared to baseline), while these increased in the placebo group: body weight 77kg → 72 kg at 3 months; waist circumference 101 → 99.8cm; and systolic BP 130 → 121.</td>
<td>Datau 2010</td>
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<td>Metabolic syndrome components</td>
<td>RDBPCT; N=123 patients</td>
<td>2g crushed Nigella seed, or placebo x 6wk</td>
<td>“Favorable impact of powdered N. sativa (Kalonji) seed in capsule was noted on almost all variables [body-mass index, waist-hip ratio, blood pressure, fasting blood sugar, lipids, ALT, and creatinine], but results were not statistically significant because of small sample size.”</td>
<td>Qidwai 2009</td>
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<td>Hypertension</td>
<td>RDBPCT; N=119 patients with hypertension below 160/100</td>
<td>100 or 200mg Nigella boiled seed extract twice daily x 8wk, or placebo</td>
<td>There was a reduction in systolic and diastolic blood pressure in both Nigella groups, in a dose-dependent manner, that was significant compared to placebo (p&lt;0.05 for all). In addition, there was a significant reduction in TC and LDL compared to baseline in the Nigella group (p&lt;0.05 for all).</td>
<td>Dehkordi 2008</td>
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<td><strong>Allergy</strong></td>
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<td>Allergic rhinitis</td>
<td>DBPCT; N=66 patients</td>
<td>Nigella oil 0.5mL x 30d, or placebo</td>
<td>N. sativa reduced the presence of the nasal mucosal congestion, nasal itching, runny nose, sneezing attacks, turbinates hypertrophy, and mucosal pallor within the first 2 weeks of treatment.</td>
<td>Nikakhlagh 2011 [Abstr]</td>
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<td>Asthma</td>
<td>RPCT; N= 29 asthma patients</td>
<td>15 mL/kg of 0.1 g% boiled aqueous seed extract daily x 3mo, or placebo solution</td>
<td>In the Nigella group the following symptoms improved significantly 3 months compared with baseline and with placebo: asthma symptoms, frequency of asthma symptoms per week, chest wheezing, and pulmonary function tests.</td>
<td>Boskabady 2007 [Abstr]</td>
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<td>Allergy</td>
<td>Report of 4 trials; N= 152 patients with allergic diseases (allergic rhinitis, bronchial asthma, atopic eczema)</td>
<td>Nigella seed oil: 1.5-4.0g per day in 500mg caps</td>
<td>Subjective report of symptoms severity improved with Nigella treatment.</td>
<td>Kalus 2003</td>
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<td><strong>Infection</strong></td>
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<td>H. pylori &amp; dyspepsia</td>
<td>RCT; N=88 patients with non-ulcer dyspepsia and positive H. pylori breath test</td>
<td>4 groups: i) triple therapy OR ii) 1, 2, or 3g Nigella in addition to omeprazole x4wk; Nigella as ground seed.</td>
<td>H. pylori eradication was 82.6, 47.6, 66.7 and 47.8% with triple therapy, and 1g, 2g, and 3g Nigella, respectively. Eradication rates [based on H pylori antibody presence in the stool] with 2g Nigella + omeprazole and triple therapy were not statistically different. Dyspepsia symptoms improved in all groups to a similar extent.</td>
<td>Salem 2010</td>
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### Acute tonsillopharyngitis

- **RDBPCT;** N=200 patients with acute tonsillopharyngitis
- **Combination of Nigella sativa 360mg and Phyllanthus niruri 50mg extract 3x/d x7d, or placebo**
- The Nigella extract led to relief of the pain and difficulty of swallowing within a few hours after the first dose. After 7 days, a significantly greater proportion of patients in the Nigella group had their sore throat completely relieved.
- **Dirjomuljono 2008 (Abstr)**

### Miscellaneous

#### Rheumatoid arthritis

- **PCT, x-over;** N=40 female RA patients; all were on combined drug therapy.
- • 1g Nigella seed oil or placebo (in 500mg caps) x 1mo
- • Disease activity improved in 42.5% and 30% of the patients respectively after Nigella.
- • The number of swollen joints and the duration of morning stiffness also improved.
- **Gheita 2012**

#### Pediatric seizure

- **DBPCT x-over;** N=22 children with refractory epilepsy
- • 1mg/kg thymoquinone from Nigella seed or placebo x 4wk
- • Thymoquinone treatment resulted in a significant reduction in seizure frequency compared to placebo (P=0.04).
- **Akhondian 2011 (Abstr)**

#### Pulmonary function

- **RDBPCT;** N=40 chemical war victims with respiratory symptoms
- • 0.375 mL/kg of 50g% boiled aqueous Nigella seed extract daily x 2mo, or placebo
- • At study end, pulmonary function tests and respiratory symptoms were significantly improved in the Nigella group compared to the control group (p < 0.01 to p < 0.001).
- • Requirements for medication were decreased in the Nigella but not the placebo group.
- **Boskabady 2008 (Abstr)**

## Safety

Based on the studies in Table 1 as well as the impressive range of activities demonstrated in preclinical research, Nigella appears to possess powerful disease modifying potential in a range of conditions. The only adverse events reported with any consistency among the trials were mild gastrointestinal upset (Akhondion 2011, Bamosa 2010, Salem 2010). Overall, Nigella and/or thymoquinone appears to have a good safety profile (Al-Ali 2008). In animals, toxicity was demonstrated only at dosages of 250 mg/kg thymoquinone by oral route (maximum tolerated dose) (Abukhader 2012). When given by intraperitoneal injection, toxicity occurred at a dose of between 15-20mg/kg thymoquinone, more than 10-fold the dose used in human trials (Abukhader 2012). Signs of toxicity were acute pancreatitis and peritonitis (Abukhader 2012). In another study, the LD50 of thymoquinone by oral administration was 870.9 mg/kg, more than 100 to 150-fold higher than the therapeutic dose (Al-Ali 2008).

## Conclusion

Nigella sativa is a highly regarded herb with a long tradition of use for infection, conditions of inflammation, respiratory and gastrointestinal conditions, and more. Human trials have demonstrated benefits from Nigella seed in metabolic conditions such as dyslipidemia, type 2 diabetes, and hypertension; and Nigella oil or extract in allergy and asthma, inflammatory conditions, infections including pharyngitis and H. pylori, as well as refractory epilepsy. Further research is needed to elucidate the potential anticancer effects of Nigella suggested by preclinical findings.

## References


